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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/043,432	LE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 14-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 14-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 8/15/05, has been entered.
Claims 12-13 have been canceled.
Claims 1-8 and 11 have been amended
Claims 14-20 have been added.

Claims 1-11 and 14-20 are pending.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's arguments, filed 8/15/05.
The rejections of record can be found in the previous Office Action, mailed 2/10/05.

3. Applicant's assertions concerning priority of the instant application have been fully considered but are not found convincing essentially for the reasons of record.

Applicant relies upon TNF-α-mediated human diseases and the disclosure of "TNF-mediated disease", "neoplastic diseases" and "malignant diseases" in priority USSN 07/670,827, filed 3/18/91, to support the recitation of "TNF α -mediated cachexia associated with cancer", as currently claimed.

It is not clear that disclosure of priority USSN 07/670,827 provides written support for "cancer" rather than "neoplastic diseases" and "malignant diseases".

It is acknowledged that the mechanism of treatment via TNF-α-specific antibodies would be the same or nearly the same (e.g. neutralizing TNF-α-mediated inflammation), regardless of the particular TNF-α – mediated disease or condition.

However, the issue of priority and new matter below is concerned with the written description of the diseases or conditions targeted in the claimed methods.

See below for a more complete analysis of the claimed recitation of "TNF α -mediated cachexia associated with cancer".

Neither the priority applications nor the instant application have provides a sufficient description of the subgenus "TNF α -mediated cachexia associated with cancer", as currently claimed.

The reliance upon the genus of "TNF-α-mediated human diseases" and the disclosure of the species "cachexia", "neoplastic diseases" and "malignant diseases" as separate entities, does not support the recitation of "TNF α -mediated cachexia associated with cancer", as currently claimed.

Applicant's arguments concerning priority of the instant claims, drawn to "TNF α -mediated cachexia associated with cancer" have not been found persuasive.

It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

It is acknowledged that the recitation of "at least one epitope ... as determined by Geysen epitope mapping ... on polypethylene pins" is disclosed in priority USSN 07/853,606, filed 3/18/92.

It is acknowledged that the recitation of "wherein said anti-TNF chimeric antibody has epitopic specificity identical to monoclonal antibody cA2" is disclosed in priority USSN 07/853,606, filed 3/18/92.

Again, if applicant desires priority prior to the instant application, applicant is invited to point out and provide documentary support for the priority of the instant claims.

Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C.§ 112, first paragraph.

Further, neither the instant specification nor the priority documents appear to provide written support for the administration of anti-TNF antibodies "via the lungs" (claim 16).

Therefore, this application repeats a substantial portion of prior USSN 09/927,703 and adds and claims additional disclosure not presented in the prior application, as indicated above. Since this application names an inventor or inventors named in the prior application, it may constitute a continuation-in-part of the prior application. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

Therefore, applicant should amend the first line of the specification to indicate the status of the instant application as a continuation-in-part.

A claim as a whole has only one effective filing date.
See Studiengelsellschaft Kahle m.b.H. v. Shell Oil Co. 42 USPQ2d 1674, 1677 (Fed. Cir 1997).

Applicant's indication that the PCT Application WO 92/16553, filed 3/18/92 and published 10/1/92, is substantially identical to priority application in USSN 07/853,606 and that the PCT Application WO 92/16553 is not in the part of applicant's priority lineage is acknowledged.

4. Claims 1-11 and 14-20 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

The specification as originally filed does not provide support for the invention as now claimed:
"TNF α -mediated cachexia associated with cancer" or
"via the lungs" (claim 16).

Applicant's amendment, filed 8/15/05, asserts that no new matter has been added and relies upon the disclosure of instant and parent applications, including the disclosure of "TNF-mediated disease", "cachexia", "neoplastic diseases" and "malignant diseases" in priority USSN 07/670,827, filed 3/18/91, to support the recitation of "TNF α -mediated cachexia associated with cancer", as currently claimed.

It is not clear that disclosure of priority USSN 07/670,827 provides written support for "cancer" rather than "neoplastic diseases" and "malignant diseases

It is acknowledged that the mechanism of treatment via TNF-α-specific antibodies would be the same or nearly the same (e.g. neutralizing TNF-α-mediated inflammation), regardless of the particular TNF-α –mediated disease or condition.

However, the issue of priority above and new matter herein is concerned with the written description of the diseases or conditions targeted in the claimed methods.

Therefore, reliance upon the genus of "TNF-α-mediated human diseases" and the disclosure of the species "cachexia" and "neoplastic disease" as separate entities, does not support the recitation of "TNF α -mediated cachexia associated with cancer", as currently claimed.

For example, Dorland's Illustrated Medical Dictionary, Twenty-Sixth Edition, W.B. Saunders Company, Philadelphia, 1980 defines cachexia as follows (see page 202, right column).

Cachexia: a profound and marked state of constitutional disorder; general ill health and malnutrition.

Cancerous cachexia: the weak, emaciated condition seen in cases of malignant tumor.

Here, "cachexia" is described generically and "cancerous cachexia" is described as an individual type or species of cachexia among a number of other types or a genus of cachexia.

It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

The instant claims now recite limitations which were not clearly disclosed in the priority applications as well as the specification as-filed, and now change the scope of the priority applications and the instant disclosure as-filed.

Therefore, reliance upon the genus of TNF-α-mediated human diseases and the disclosure of the species or subgenus of "TNF α -mediated cachexia associated with cancer", does not support the recitation of "TNF α -mediated cachexia associated with cancer", as currently claimed.

The disclosure of "anti-TNF peptides of Mabs of the present invention can be administered by any means that enables the active agent to reach the agent's site of action in the body of a mammal. ... absorption." on page 59, lines 23-29 of the instant specification does not provide sufficient written support of "via the lungs" as currently claimed.

Again, it is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

The specification as filed does not provide a sufficient written description or set forth the metes and bounds of this phrase. The specification does not provide blazemarks nor direction for the instant methods encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02 and 2163.06

5. Claims 1, 3-5, 11 and 14-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

It is apparent that the cA2 antibody is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the cell line / hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

Applicant's arguments and comments, filed 8/15/05, concerning the enablement of the cA2 antibody is acknowledged.

Applicant's reliance upon the prosecution in priority USSNs to establish compliance with the deposit of biological materials under 35 USC 112, first paragraph, enablement as wells In re Wands, 8, USPQ2d 1400 (CAFC 1988) is acknowledged.

However, biological materials must be known and readily available to the public . Neither concept alone is sufficient. See MPEP 2404.01.

Even a deposit made under the Budapest Treaty and referenced in a United States of foreign patent document does not necessarily meet the test for known and readily available unless the deposit was made under conditions that are consistent with those specified in the rules. (See MPEP 2404.01).

Also, it is noted that the claims are drawn to the particular chimeric cA2 antibody and not the mouse A2 antibody.

It is noted that the sequence of an entire immunoglobulin satisfies the biological deposit of said immunoglobulin. Note that satisfaction for the biological deposit of the specific cA2 antibody requires the disclosure and recitation of its entire amino acid sequence and **not** based upon partial sequences.

While applicant has noted that in addition to disclosing the heavy / light chain variable sequences and methods of production of chimeric anti-TNF antibodies,
the recitation of "cA2" requires the enablement of this particular "cA2" antibody and not chemically and structurally similar cA2-specific antibodies.

Given applicant's arguments concerning the structure of the particular cA2 antibody, applicant is invited to claim the cA2 antibody via sequences that read on the entire particular cA2 antibody.

In the absence of a clear recitation in the claims that reads on the exact structure of the cA2 antibody, the rejection is maintained.

Unlike Wands, this is not a case of making antibodies to a particular specificity by screening a number of possible positive clones. **Rather, the issue is the structure of a particular antibody, namely cA2, and not on a genus of TNF-specific antibodies.**

It is noted that it is unclear if a cell line which has the exact structural and chemical identity of the cA2 antibody can be reproducibly isolated without undue experimentation. Replication of the claimed chimeric cA2 antibody is an unpredictable event. Further, a particular biological material or cell line can undergo changes resulting in microheterogeneity. Therefore, a suitable deposit or alternative means for patent purposes is required. Without a publicly available deposit of the appropriate cell line for the claimed cA2 antibody or a clear recitation of the structure of the claimed cA2 antibody, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed.

As indicated previously, given the disclosure and the claims encompassing the instant cA2 antibody set forth in U.S. Patent No. 5,919,452; the conditions for the enablement of biological materials under 35 USC 112, first paragraph, with respect to cA2 appear to have been satisfied.

However in the interest of clarity and compact prosecution, again applicant is required to make the record clear exactly what is the scope of the instantly claimed cA2.

It is noted that the requirements under 35 USC 112, first paragraph, for the claimed cA2 antibody was not satisfied by the deposit of the cA2 antibody in the priority applications, some of which are patented now.

However, the instant record should indicate the parameters that have satisfied the enablement requirements under 35 USC 112, first paragraph, for the cA2 antibody.

6. Applicant's amended claims in conjunction with applicant's arguments, filed 8/15/05 have obviated the previous rejection under 35 U.S.C. 112, first paragraph, enablement, with respect to the "TNF-α specificity".

7. Claims 1, 3-5, 11 and 14-20 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1, 3-5, 11 and 14-20 are indefinite in the recitation of "cA2" because its characteristics are not known. The use of "cA2" monoclonal antibody as the sole means of identifying the claimed antibody renders the claim indefinite because "cA2" is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation s to define completely distinct hybridomas / cell lines.

Applicant is invited to clarify the metes and bounds of the claimed cA2 antibody.

Applicant's arguments and comments, filed 8/15/05, have been fully considered concerning the indefiniteness of the instant "cA2".

However in the interest of clarity and compact prosecution, again applicant is required to make the record clear exactly what is the metes and bounds of the instantly claimed cA2.

As indicated previously and above,
given the disclosure and the claims encompassing the instant cA2 antibody set forth in U.S. Patent No. 5,919,452; the conditions for the enablement of biological materials under 35 USC 112, first paragraph, with respect to cA2 appear to have been satisfied.
Applicant is invited to clarify the instant record.

It is noted that the requirements under 35 USC 112, first and second paragraphs, for the claimed cA2 antibody have been satisfied in the priority applications, some of which are patented now.

However, the instant record should indicate the parameters that have satisfied the requirement under 35 USC § 112, second paragraph as well as the enablement requirements under 35 USC 112, first paragraph, for the cA2 antibody.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

8. Claims 1-11, 14-15 and 17-20 are rejected under 35 U.S.C. § 102(b) as being anticipated Le et al. (WO 92/16553) (1449; #AN4) (see entire document) essentially for the reasons of record

Le et al. teach treating cachexia associated with cancer in humans (e.g. see page 3, paragraph 1; page 8, paragraph 3; pages 13-15, page 20, page 22, page 34) by administering the recombinant cA2 antibody (e.g. see pages 9-11; page 13, paragraph 1 and Examples on pages 45- 74) of the instant invention (see entire document, including Description of the Prior art, Summary of the Invention, Detailed Description of the Preferred Embodiments and Claims). In addition, Le et al. teach the determination of amino acid sequences of cA2-specific epitopes via Geysen epitope mapping (See Examples XIII – XIV on pages 62 – 70). Given the teaching of antibodies that bind the epitope that are recognized by the cA2 anti-TNF antibody as well as the cA2 antibody itself, the prior art teaches antibodies that bind the identical epitope of the cA2 antibody. Given the prior art teachings drawn to the same chimeric cA2 antibodies and/or the same cA2 starting materials, the specific antibody regions comprising SEQ ID NOS: 2, 3,4 and/or 5 would be inherent properties of said recombinant cA2 antibodies.

Le et al. also teach modes (e.g. parenteral, iv, subcutaneous, intramuscular, oral) and dosages of administration (e.g. single, divided) as well as combination therapy with other antibodies, lymphokines, growth factors that anticipate the claimed methods as well (see pages 34-37).

It appears that the prior art methods do not result in a manipulative difference between the prior art and the claimed methods.

Applicant's arguments and the examiner's rebuttal concerning the priority of the instant recitation of "cachexia associated with cancer" are addressed above in the discussion of priority and the new matter rejection under 35 USC 112, first paragraph.

10. Claims 1 and 16 are rejected under 35 U.S.C. § 103(a) as being unpatentable over anticipated Le et al. (WO 92/16553) (1449; #AN4) (see entire document).

Le et al. is taught above and differs from the claimed methods by not disclosing "administration via the lung".

Depending on the needs of the patient and the nature of the therapeutic endpoint as known and practiced by the ordinary artisan and taught by Le et al. (e.g. see pages 34-47; "administered by any means that enable the active agent to reach the agent's site of action in the body of a mammal"; "chosen route of administration and standard pharmaceutical practice" one of ordinary skill in the art at the time the invention was made would have been motivated to provide antagonistic antibodies via multiple modes of administration, including the pulmonary routes of administration as known and practiced at the time the invention was made. A person of ordinary skill in the art would have recognized that treating various inflammatory conditions with anti-TNF antibodies as discussed by the prior art references would be appropriate for a number of inflammatory conditions, including "cachexia associated with cancer" as a pathology associated with pro-inflammatory TNF at the time the invention was made.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. Claims 1-11 and 14-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of copending USSN 10/957,134 and claims 1-70 of copending USSN 10/957,549 essentially for the reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because it appears that the same or nearly the same cancer patients are being targeted with the same or nearly the same cA2 TNF-specific antibodies. While the instant claims are drawn to treating cachexia associated with cancer, it appears that the instant claims anticipate or render obvious treating the same or nearly the same cancer patients of the copending applications. Further, the additional dosing and therapeutic regimens recited in the copending claims appear to be standard therapeutic regimens for cancer patients at the time the invention was made. The disclosure of all of these pending applications acknowledge that the extensive wasting associated with cancer known as cachexia is a TNF-mediated disease.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant will provide a terminal disclaimer upon resolution of the remaining rejections.

12. Claims 1-11 and 14-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 5,919,452 in view of the acknowledgement that cachexia associated with cancer is TNF-mediated disease other than a disease resulting from infection as acknowledged on page 3, paragraph 1 of the instant specification essentially for the reasons of record. The instant claims anticipate the patented claims. When the patented claims are read in light of the instant specification (page 3) and the patent specification columns 1-2, overlapping paragraph), applicant appears to acknowledge that the extensive wasting associated with cancer know as cachexia is a TNF-mediated disease encompassed by the patented method claims.

Applicant did not address this obviousness-type double patenting of record.

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

PHILLIP GAMBEL

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